Notice of Allowability	Application No.	Applicant(s)	
	09/844,655	HUANG ET AL.	
	Examiner	Art Unit	
	Jacob Cheu	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *2/4/2005*.

2. ☒ The allowed claim(s) is/are *94-97, 99-105, 108-117 now renumbered as 1-21*.

3. ☐ The drawings filed on _____ are accepted by the Examiner.

4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☒ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☐ Examiner's Amendment/Comment
8. ☐ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

EXAMINER'S AMENDMENT

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Mr. Abney on April 14, 2005.

The application has been amended as follows:

Please replace claims 94-117 with the following:

94. (Previously Presented) A method of detecting the activity of an enzyme that performs a phosphate modification on a substrate to form a product in a sample, comprising:

contacting the substrate with the enzyme in the sample;

contacting the sample with a binding partner that specifically binds to the substrate or to the product, but not to both, wherein the binding partner includes **Ga(III) ion** ~~gallium~~ that is required for binding between the binding partner and the substrate or the product;

detecting a response, based on luminescence polarization, indicative of the extent of binding between the substrate or the product and the binding partner without separating the bound substrate or product from the unbound substrate or product; and

correlating the response with the activity of the enzyme.

95. (Original) The method of claim 94, wherein the step of detecting a response comprises:

exposing the sample to polarized light; and

measuring the degree of polarization of light emitted from the sample, in response to the step of exposing, wherein the degree of polarization is indicative of the extent of binding between the substrate or product and the binding partner.

96. (Original) The method of claim 95, further comprising determining the degree of polarization of the emitted light using a function selected from the group consisting of polarization and anisotropy.

97. (Previously Presented) The method of claim 94, wherein the substrate is a polypeptide, and wherein the substrate and product are related by phosphorylation or dephosphorylation of the polypeptide.

98. (Canceled)

99. (Previously Presented) The method of claim 97, wherein the substrate and product are luminescent.

100. (Previously Presented) The method of claim 99, wherein the enzyme is a kinase, wherein the product is related to the substrate by phosphorylation of the substrate, wherein the binding partner specifically binds to the product but not to the substrate, and wherein the degree of polarization of light emitted from the sample is higher when the enzyme is operative to form the product from the substrate than when the enzyme is inoperative or absent.

101. (Previously Presented) The method of claim 99, wherein the enzyme is a phosphatase, wherein the product is related to the substrate by dephosphorylation of the substrate, wherein the binding partner specifically binds to the substrate but not to the product, and wherein the degree of polarization of light emitted from the sample is lower when the enzyme is operative to form the product from the substrate than when the enzyme is inoperative or absent.

102. (Original) The method of claim 94, wherein the substrate is a nucleotide, and wherein the substrate and product are related by a cyclization or decyclization of the nucleotide.

103. (Original) The method of claim 102, wherein the substrate and product are luminescent.

104. (Original) The method of claim 103, wherein the enzyme is a phosphodiesterase, wherein the substrate is a cyclic nucleotide, wherein the product is a nucleotide monophosphate formed by decyclization of the substrate, wherein the binding partner specifically binds to the product but not to the substrate, and wherein

the degree of polarization of light emitted from the sample is higher when the enzyme is operative to form the product from the substrate than when the enzyme is inoperative to absent.

105. (Original) The method of claim 103, wherein the enzyme is a cyclase, wherein the substrate is a nucleotide monophosphate, wherein the product is a cyclic nucleotide formed by cyclization of the substrate, wherein the binding partner specifically binds to the substrate but not to the product, and wherein the degree of polarization of light emitted from the sample is lower when the enzyme is operative to form the product from the substrate than when the enzyme is inoperative or absent.

106. (Canceled)

107. (Canceled)

108. (Original) The method of claim 94, wherein the enzyme is selected from the group consisting of kinases and phosphatases.

109. (Original) The method of claim 94, wherein the enzyme is selected from the group consisting of cyclases and phosphodiesterases.

110. (Original) The method of claim 94, wherein the substrate includes a phosphorylated polypeptide or a nonphosphorylated polypeptide.

111. (Original) The method of claim 94, wherein the substrate includes a cyclized nucleotide or a noncyclized nucleotide.

112. (Original) The method of claim 94, further comprising:

contacting the substrate and enzyme with a candidate compound; and

determining the ability of the candidate compound to enhance or inhibit enzyme activity by its effects on the response.

113. (Original) The method of claim 94, the binding between the binding partner and the substrate or product being characterized by a binding coefficient, wherein the binding coefficient is no larger than about 10^{-8} M.

114. (Original) The method of claim 94, further comprising:

providing a sample holder having a plurality of sample sites supporting a corresponding plurality of samples; and

repeating the steps of contacting, detecting, and correlating for each of the plurality of samples.

115. (Previously Presented) The method of claim 94, wherein the step of contacting the substrate with the enzyme precedes the step of contacting the sample with a binding partner.

116. (New) The method of claim 94, the step of contacting the substrate with the enzyme catalyzing a reaction that forms the product, wherein the response is determined at least substantially at an end point of the reaction.

117. (New) The method of claim 94, the step of contacting the substrate with the enzyme catalyzing a reaction that forms the product, wherein the response is determined at different times along the time course of the reaction.

2. The following is an examiner's statement of reasons for allowance: no prior art teaches or suggests Ga(III)-based enzymatic assay by using luminescence polarization as the instant invention. The closest prior arts are references of Nikiforov (USP 6472141) and Posewits et al. (Anal. Chem. 1999, Vol. 7: 2883-2892). Nikiforov et al. teaches a fluorescence polarization assay to determine the phosphorylation of a phosphoryatable compound, i.e. phosphotase (dephosphorylate) or kinase (phosphorylate) on the polypeptide substrate. (Col. 3, line 7-20) However, Nikiforov does not specifically teach using gallium (Ga) metal ion for its fluorescent polarization assay. And such deficiency cannot be rescued by the teaching of Posewits et al. because Posewits et al. teach that Fe(III) is far better than Ga(III) in binding of the bound phosphorylated peptides. Thus, one ordinary skill in the art would not contemplate using Ga instead of Fe for a better result in the enzymatic binding assay.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue

fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jacob Cheu whose telephone number is 571-272-0814. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jacob Cheu
Examiner
Art Unit 1641

April 15, 2005

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

04/18/05